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Trends in the use of antidepressants among older adults: Bambuí Project

Tendências no uso de antidepressivos entre idosos mais velhos: Projeto Bambuí

ABSTRACT

OBJECTIVE: To analyze the trends and factors associated with the antidepressant use among older adults.

METHODS: This population-based study evaluated older adults in 1997 (n = 351, baseline) and the survivors at the 15th follow-up year (n = 462, in 2012) among the aging cohort of Bambuí. The prevalence of antidepressant use was estimated, and the most commonly used antidepressants each year were identified. Prevalence ratios with 95% confidence intervals were estimated using Poisson regression with robust variance to investigate differences in the prevalence of use between 1997 and 2012.

RESULTS: The overall consumption of antidepressants (PR = 2.87, 95%CI 1.94;4.25) and of selective serotonin reuptake inhibitors (PR = 7.50, 95%CI 3.74;15.02) was significantly higher in 2012. However, no significant difference was observed in the use of tricyclic antidepressants between the two cohorts (PR = 0.89, 95%CI 0.49;1.62). In the 2012 cohort, antidepressant use was associated with females, increased age, increased income (≥ 4 minimum wages), self-assessment of health as reasonable, and attending ≥ 5 medical consultations in the last 12 months.

CONCLUSIONS: The increased consumption of antidepressants in the period due to increased use of selective serotonin reuptake inhibitors was consistent with results observed in international studies of different population groups and contexts. The positive correlation observed between antidepressant use and family income may be a warning of possible inequalities in access to mental health services.

DESCRIPTORS: Aged. Antidepressive Agents, therapeutic use. Drug Utilization, trends. Socioeconomic Factors. Pharmacoepidemiology.

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RESUMO

OBJETIVO: Analisar a tendência e os fatores associados ao uso de antidepressivos por idosos mais velhos.

MÉTODOS: Estudo de base populacional com idosos integrantes da linha base ($n = 351$, em 1997) e dos sobreviventes no 15º seguimento ($n = 462$, em 2012) da coorte idosa de Bambuí. Estimou-se a prevalência do consumo de antidepressivos e foram identificados os antidepressivos mais consumidos em cada ano. Razões de prevalência com intervalos de confiança de 95% foram estimadas por meio da regressão de Poisson, com variância robusta, na investigação de diferenças de prevalência no uso do medicamento entre os dois anos.

RESULTADOS: O consumo global de antidepressivo ($RP = 2,87$; $IC95\% 1,94;4,25$) e do grupo dos inibidores seletivos da recaptura da serotonina ($RP = 7,50$; $IC95\% 3,74;15,02$) foi significativamente maior em 2012. Entretanto, não foi observada diferença significativa no consumo de antidepressivos tricíclicos entre as duas coortes ($RP = 0,89$; $IC95\% 0,49;1,62$). Na coorte recente (2012), o uso de antidepressivos mostrou-se associado ao sexo feminino, à idade e à renda (≥ 4 salários mínimos) mais elevadas, à autoavaliação da saúde como razoável e à realização de cinco ou mais consultas médicas nos últimos 12 meses.

CONCLUSÕES: O crescimento do consumo de antidepressivos no período, devido ao aumento no uso dos inibidores seletivos da recaptura da serotonina, mostrou-se consistente com o observado em estudos internacionais, com diferentes populações e contextos. A associação positiva observada em relação à renda alerta para possível desigualdade no acesso aos serviços de saúde mental.

DESCRIPTORIOS: Idoso. Antidepressivos, uso terapêutico. Uso de Medicamentos, tendências. Fatores Socioeconômicos. Farmacoepidemiologia.

INTRODUCTION

Antidepressants (AD) are considered the treatment of choice in acute manifestations of moderate to severe depression for improvement or complete remission of symptoms.⁹ AD are also used in the management of other health problems, including anxiety disorders and chronic pain.¹⁵

International population-based studies have identified growth in AD use, both in the general adult population^{2,17} and among older adults.^{8,12} This growth is due to greater use of selective serotonin reuptake inhibitors, which are gradually replacing tricyclic AD as the most commonly used chemical subgroup.^{2,13,17}

To date, only one Brazilian study²⁰ has evaluated the trends in AD consumption among different population groups. It was conducted in a mid-sized city in Southern Brazil, and it evaluated the use of psychotropic drugs in the adult population aged ≥ 15 years between 1994 and

2003. The authors reported a significant increase from 8.4% to 31.6% in AD use. However, this difference was not adjusted for sample characteristics that could be associated with the consumption of AD. Other Brazilian studies have investigated AD use at the population level in terms of prevalence and associated factors. However, they evaluated the overall adult population.^{6,10,19}

The presence of chronic comorbidities is a common condition among older adults, and depression is among the chronic diseases that often affects this population.⁵ Older adults are the main consumers of AD^{6,20,23} and consumption among older adults is higher than that in their younger counterparts.³ Considering the rapid aging of the Brazilian population, the challenges this phenomenon poses to pharmaceutical care, and the limited number of studies on this topic, this study aimed to evaluate the trend and factors associated with AD use among older adults.

METHODS

This study is a substudy of the Bambuí Project, a longitudinal study investigating the incidence and predictors of health outcomes among older adults in a community living situation. Details of the methodology used have been presented in a previous publication.¹⁶

The aforementioned study¹⁶ was conducted in the city of Bambuí, located in Southwestern state of Minas Gerais, with 15,000 inhabitants in 1997, when the baseline cohort was evaluated by a census of older adults living in the city. In the present study, the older adults considered eligible to participate were aged between 75 and 89 years who were among the baseline of the 1997 cohort (born between 1908 and 1922), herein designated the 1997 cohort, and the survivors of this same cohort in 2012, herein designated the 2012 cohort, in the same age group (born between 1923 and 1937).

The dependent variable was AD use reported by participants in interviews when the drug label and medical prescription were also examined. The medications were identified and their active principles were classified according to the Anatomical Therapeutic Chemical Index^a (ATC).

The medications listed in ATC under code N06A were considered AD. In addition, AD were classified according to their chemical subgroup (ATC level 4) and chemical substance (ATC level 5).

The independent variables included sociodemographic characteristics, health conditions, and descriptors of the use of health care services. Sociodemographic characteristics included sex, age, education (none, 1-3, and ≥ 4 full years), marital status (married/consensual union, widowed, divorced/single), family income (< 2.0 , 2.0-3.9, and ≥ 4.0 minimum wage equivalents), and living status (living alone, not living alone). The minimum wage was equivalent to US\$120.00 in 1997 and US\$333.00 in 2012. The health conditions investigated included the presence of common mental disorders (depression and anxiety), self-assessment of health, number of chronic diseases, and functional disability. The common mental disorders were evaluated using the 12-item version of the General Health Questionnaire (GHQ-12),¹¹ and individuals with scores ≥ 5 points were considered positive. Self-assessment of health was based on the answer to the question: "How would you rate your health?" (very good/good; reasonable; poor). The chronic health conditions evaluated were hypertension, diabetes, Chagas disease, heart attack, and stroke, and they were measured on the basis of the patients' medical diagnostic reports. With regard to functional capacity, older adults were considered functionally disabled if they experienced

difficulty or were unable to perform at least one of the following basic activities of daily living without help: getting out of bed, eating, walking from one room to another, and bathing. Hospitalization history, number of medical consultations over the past 12 months, and health insurance coverage were the descriptor variables related to the use of health care services.

Data were collected in the homes using questionnaires administered by the interviewers. Interviewers were recruited from the community, had education superior to 11 years, and were trained by the research team, ensuring consistency in applying the instruments and collecting the data in 1997 and 2012.

The prevalence of AD use (overall and by chemical subgroup) was calculated separately for each birth cohort by dividing the number of older adults reporting AD consumption by the total number of cohort members. In the evaluation of the chemical subgroups and most commonly used active ingredients, the medication was considered the unit of analysis. Therefore, the ratios were calculated by dividing the total number of AD in each chemical subgroup or active principle by the total number of AD reported. The chemical subgroups considered were selective serotonin reuptake inhibitors (SSRI), tricyclic AD (TCA), and monoamine oxidase inhibitors (MAOI). The Chi-square test was used to compare the two birth cohorts in relation to the variables evaluated. The factors associated with AD use (global) in each birth cohort were evaluated using Poisson regression with robust variance to estimate the prevalence ratios and 95% confidence intervals. The inclusion of a covariate in the statistical model was not influenced by the results of the univariate analyses. The same analytical strategy was used to test the hypothesis of association between the year of the cohort and AD use (overall and by chemical subgroup). However, to determine the differences in the prevalence of use between the 1997 and the 2012 cohorts, only the variables independently associated with AD use in at least one of the cohorts were included in the multivariate model. In all analytical steps, a significance level of 5% was used. Data analysis was performed using Stata[®] version 10 statistical software (Stata Corp., College Station, USA).

The Bambuí Project was approved by the Research Ethics Committee of the René Rachou Research Center (Opinion 346,329 – CAAE 01082212.7.0000.5091). All participants from both cohorts signed a free and informed consent form.

RESULTS

The 1997 cohort ($n = 351$) and the 2012 cohort ($n = 462$) were similar in age (means of 79.8 and 79.9 years,

^a World Health Organization. Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2013. Geneva; 2013. Available from: http://www.whocc.no/atc_ddd_index

respectively), sex (60.1% and 66.5% were females, respectively), and marital status (50.4% and 57.7% were widowed, respectively). When compared with the 1997 cohort, the 2012 cohort had higher education and income ($p < 0.001$ for both variables), lower prevalence of depressive disorders, less disability for at least one basic activity of daily living, better self-assessment of health ($p < 0.001$), better health insurance coverage ($p < 0.001$), and higher frequency of medical consultations in the past 12 months ($p = 0.014$), although members of this cohort were hospitalized less during in the same period ($p = 0.048$). The complete characterization of the two cohorts can be observed in Table 1.

AD use increased from 8.3% in 1997 to 23.6% in 2012, and this trend was observed in both sexes and in all age groups. In both cohorts, consumption was higher among females and increased with age, except among the older male adults of the 1997 cohort, whose consumption was stable across the age groups (Figure).

With regards to the pharmacological classes, changes in the consumption pattern were observed between the two cohorts; the consumption of TCA prevailed in the 1997 cohort, accounting for 69.0% of total AD consumption, whereas the consumption of SSRI prevailed in the 2012 cohort, accounting for 68.1% of total AD consumption. The use of MAOI was observed only in the 1997 cohort and the use of other AD (code N06AX) was restricted to the 2012 cohort. However, in both cohorts, the consumption of these chemical groups was lower than that of TCA and SSRI. Citalopram was the most frequently used active ingredient, corresponding to 31.1% of total consumption in the 2012 cohort, whereas no active ingredient predominated in the 1997 cohort (data not shown).

In the 2012 cohort, the following factors were positively associated ($p < 0.05$) with AD use after univariate analysis: female sex, age, and family income (among the sociodemographic characteristics), presence of depressive disorders, self-assessment of health as poor (among the health conditions), having two or more medical consultations, and type of health insurance coverage (among the characteristics pertaining to the use of health care services). The following variables were positively associated with AD use after multivariate analysis: female sex, family income ≥ 4 minimum wage equivalents, self-assessment of health as reasonable, and having five or more medical consultations in the last 12 months (Table 2). In the 1997 cohort, having five or more medical consultations was the only variable positively associated with AD use using both univariate and multivariate analyses (OR = 4.41, 95%CI 1.21;16.1) (data not shown).

Table 3 shows the results of univariate and multivariate analyses for the association between birth cohorts and AD use (overall and for the two most commonly used

chemical subgroups). Even after adjusting for sex, age, family income, self-assessment of health, and number of medical consultations, the overall consumption of AD and SSRI was significantly higher in the 2012 cohort. However, no significant difference was observed in the consumption of TCA between the two cohorts. Considering that AD use differed between older males and females, a trend analysis was conducted to evaluate medication use stratified by sex. However, the results obtained within each stratum did not differ from those observed in the total population.

DISCUSSION

This study identified a significant increase in AD use between 1997 and 2012, primarily due to increased consumption of SSRI. In both cohorts and in all age groups, consumption of AD was higher among females. In the 2012 cohort, in addition to females, increased age and income, self-assessment of health as reasonable, and attending five or more medical consultations in the past 12 months were positively associated with AD use.

Between 1997 and 2012, the consumption of AD by older adults from Bambuí significantly increased approximately three fold, regardless of the characteristics associated with their use in this cohort. Growth in the consumption of AD has also been observed in higher-income countries among the general adult^{2,17} and older adult population.^{4,8,12,13} A Brazilian population-based study showed a significant increase in AD use from 8.4% to 31.6% but included not only the older groups but all residents aged ≥ 15 years.²⁰

Previous studies have elucidated the reasons for the growing AD use, and these reasons are not mutually exclusive. The most obvious reason is the increased prevalence of depression in the older population.¹ In fact, in addition to improved diagnosis of depressive disorders by healthcare professionals,^{2,20} depression in the final stage of life is a common event among older adults owing to the presence of chronic diseases, impaired functional capacity, loneliness, and decreased social support network.^{1,13} Another cause would be extended drug treatment for depression, particularly among those with a history of multiple depressive episodes. This has also been observed in international studies, whether based on primary data^{14,21,22} or on databases of consultations and medical prescriptions.¹⁸ A third cause is growing acceptance among healthcare professionals and patients of the new generation of AD such as SSRI, which have fewer side effects and are better tolerated and safer than TCA and MAOI (older class), particularly in overdose situations.¹⁴ The fact that depressive older adults are commonly treated with drugs at the expense of other therapeutic options, such as psychotherapy, also should not be discarded.²⁴

Table 1. Comparison of the profile of the 1997 cohort (baseline) and survivors (2012 cohort) in Bambuí, state of Minas Gerais, Southeastern Brazil.

Variable	1997 (N = 351)	2012 (N = 462)	p
Age in years ^a	79.8 (3.7)	79.9 (3.8)	0.712
Sex			
Male	39.9	33.6	0.063
Female	60.1	66.5	
Education (years completed)			
0	39.0	24.7	< 0.001
1 to 3	29.6	36.6	
≥ 4	31.4	38.7	
Marital status			
Married/Consensual union	36.5	33.4	0.056
Widowed	50.4	57.7	
Single or divorced	13.1	8.9	
Family income (in minimum wage equivalents)			
< 2.0	35.1	20.9	< 0.001
2.0 to 3.9	34.3	44.6	
≥ 4.0	30.6	34.6	
Lives alone			
No	80.1	73.3	0.025
Yes	19.9	26.7	
Depressive disorders			
No	57.2	80.7	< 0.001
Yes	42.8	19.3	
Self-assessment of health			
Very good/Good	31.9	53.5	< 0.001
Reasonable	45.9	37.5	
Poor	22.2	9.1	
Number of chronic diseases			
0	35.0	14.2	< 0.001
1	43.0	46.4	
≥ 2	22.0	39.4	
Inability to perform at least one basic activity of daily living			
No	75.6	85.0	0.001
Yes	24.4	15.0	
Number of medical consultations in the last 12 months			
0 to 1	33.1	23.8	0.014
2 to 4	40.2	46.3	
≥ 5	26.8	29.9	
Hospitalization history in the past 12 months			
No	71.8	77.9	0.048
Yes	28.2	22.2	
Health insurance coverage			
No	82.6	66.6	< 0.001
Yes	17.4	34.4	

^a Mean (SD).

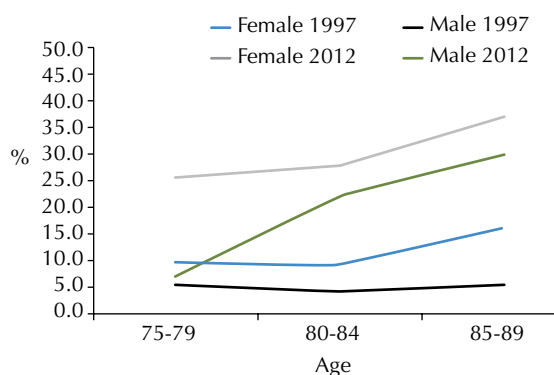


Figure. Antidepressant use by sex and age among individuals aged 75-89 years. Bambuí, MG, Southeastern Brazil, 1997 and 2012.

In line with the results of international population-based studies,^{2,17,25} the increased consumption of AD in Bambuí was primarily due to the increased use of SSRI, considering that the consumption of TCA was similar between the two cohorts. The prevalence of SSRI among AD used by the 2012 cohort is consistent with that observed in Brazil^{6,19} and other countries.²² This result indicates the possibility that among the older people of Bambuí, increased consumption of AD results from greater acceptance of SSRI by professionals and patients. After the appearance of this chemical subgroup, general practitioners have more frequently prescribed AD, a practice that used to be restricted to psychiatrists.¹⁷ It is noteworthy that only 1.0% of the population consulted a psychiatrist. Furthermore, a negative correlation was observed between the increased prevalence of AD consumption and depression in the 2012 cohort. This may be due to adequate treatment among older adults in the 2012 cohort, resulting in improvement or remission of depressive symptoms and consequently a negative rating for the GHQ-12. This may also be a consequence of AD use in the management of other health problems, such as anxiety disorders and other chronic diseases.⁴

The identification of independent factors associated with AD use was largely confined to the 2012 cohort. In the 1997 cohort, the only characteristic associated with AD use after multiple adjustments was the number of medical consultations.

The consumption of AD was higher among females. International^{12,14,17,25} and Brazilian studies^{6,10,19} have shown an association between females and AD use. Some authors argue that the higher consumption of AD among females is due to the increased prevalence of depressive disorders in this group.^{6,10,17} However, in the present study, the association between females and AD use remained significant regardless of the presence of depressive disorders. Grunenbaum¹² (2008) draws attention to the possibility of feminization of depression, because females

identify psychiatric conditions and pursue treatment for these disorders more intensely than males. In this study, the consumption of AD did not significantly differ between males and females presenting with depressive disorders, but was significantly different among those without depressive disorders (data not shown). This result could indicate that, in Bambuí, older females use AD to treat health problems other than depression, such as anxiety disorders, sleep disturbances, physical problems, and even social problems caused by the difficulties experienced in daily life.²⁵ Alternatively, females may adhere to the pharmacological treatment of depression more often than males.

Other sociodemographic characteristics associated with AD use were increased age and higher income. A positive association between age and AD use was observed in other older groups.^{13,25} General practitioners have reported depression at the end of life as a spectrum that includes loneliness, lack of social network, and impaired functionality.¹³ As for the positive association between income and AD use, increased access to medications could be due to greater ability to bear health costs among those with better socioeconomic status.¹⁰ In Bambuí, the prevalence of depressive disorders was higher among the lower income strata (data not shown), which raises concerns about possible inequalities in mental health care in this population segment due to its limited access to mental health care services.⁶

In the case of descriptive variables related to health conditions and use of health care services, only the self-assessment of health (in the first case) and the number of medical consultations (in the second) were associated with AD use after adjusting for other covariables. The positive association between consumption of AD and worse self-assessment of health (even restricted to assessment as "reasonable") is consistent with results observed among older Australian adults²⁵ and indicates the importance of subjective assessment of health in determining AD use. The positive association between consumption of AD and the number of medical consultations is related to the need for a prescription from a medical professional in order to obtain the drug.

One limitation of this study is the inability to assess the appropriate AD use with regard to drug indication and dosage, owing to the lack of use of a gold standard method for diagnosing depression as well as the unavailability of data on duration of use/dosage for medications and access to psychotherapy. The GHQ-12¹¹ screening tool used to evaluate common mental disorders in the study population showed the same accuracy as the 30-item Geriatric Depression Scale (GDS-30) in diagnosing depressive symptoms.⁷ However, the GHQ-12 only verifies the presence of symptoms of depression and does not define clinical diagnosis. Moreover, the cutoff value used to classify the participants as positive did not allow differentiation

Table 2. Results of univariate and multivariate analyses of factors associated with antidepressant use among individuals aged 75-89 years. Bambuí, MG, Southeastern Brazil, 2012.

Characteristics	%	PR _{raw}	95%CI	PR _{adjusted}	95%CI
Age	80.7 (4.0) ^a	1.06	1.01;1.10	1.05	1.01;1.09
Sex					
Male	14.8	1.00		1.00	
Female	28.0	1.89	1.24;2.87	1.77	1.11;2.82
Education (years completed)					
None	19.3	1.00		1.00	
1 to 3	29.4	1.29	0.81;2.04	1.43	0.87;2.35
≥ 4	25.1	1.30	0.83;2.05	1.33	0.78;2.26
Marital status					
Married/Consensual union	19.5	1.00		1.00	
Widowed	26.7	1.37	0.94;2.00	1.02	0.66;1.58
Single or divorced	19.5	2.00	0.50;2.02	1.02	0.53;1.97
Family income (in minimum wages)					
< 2.0	18.2	1.00		1.00	
2.0 to 3.9	20.0	1.07	0.65;1.76	1.40	0.82;2.39
≥ 4.0	30.2	1.61	1.00;2.60	1.93	1.08;3.45
Lives alone					
No	23.0	1.00		1.00	
Yes	23.8	1.03	0.71;1.50	1.33	0.82;2.13
Depressive disorders					
No	20.9	1.00		1.00	
Yes	34.8	1.67	1.18;2.36	1.26	0.86;1.86
Self-assessment of health					
Very good/Good	18.2	1.00		1.00	
Reasonable	29.5	1.62	1.14;2.30	1.62	1.13;2.32
Poor	31.0	1.70	1.01;2.87	1.50	0.83;2.70
Number of chronic diseases					
None	24.6	1.00		1.00	
1	24.1	0.98	0.60;1.59	0.80	0.50;1.26
≥ 2	23.3	0.95	0.57;1.57	0.74	0.45;1.22
Inability to perform at least one basic activity of daily living					
No	22.1	1.00		1.00	
Yes	31.9	1.45	0.98;2.14	1.01	0.65;1.59
Number of medical consultations					
0 to 1	12.7	1.00		1.00	
2 to 4	23.8	1.87	1.09;3.23	1.61	0.92;2.82
≥ 5	31.9	2.51	1.45;4.33	2.10	1.16;3.81
Hospitalization history					
No	22.0	1.00		1.00	
Yes	27.7	1.26	0.87;1.83	1.07	0.69;1.64
Health insurance coverage					
No	20.0	1.00		1.00	
Yes	31.4	1.57	1.13;2.17	1.37	0.95;1.97

Raw and adjusted PR (for all variables described in the table) estimated using Poisson regression model with robust variance.

^a Mean (SD).

Table 3. Antidepressant use among older adults aged 75-89 years. Bambuí, MG, Southeastern Brazil, 1997 and 2012.

Antidepressant use	1997	2012	PR _{raw}	95%CI	PR _{adjusted} ^a	95%CI
Global (%)	8.3	23.6	2.86	1.94;4.20	2.87	1.94;4.25
Tricyclic compounds (%)	5.7	5.6	0.99	0.56;1.74	0.89	0.49;1.62
Selective serotonin reuptake inhibitors (%)	2.3	17.3	7.60	3.62;15.05	7.50	3.74;15.02

Estimation of PR using Poisson regression with robust variance.

^a Adjusted for sex, age, family income, self-rated health assessment, and number of medical consultations.

between mild or severe symptoms. For the first case, psychotherapy is indicated, whereas drug therapy is the first choice in cases of severe depression.⁹ Another limitation is the impossibility of verifying whether AD was prescribed by a psychiatrist. The present results cannot be generalized to other older groups, particularly those attending geriatric day hospitals or nursing homes. However, the study has advantages, particularly when compared with studies on drug dispensing or those based on prescriptions because it uses data on drug use. In addition, the accuracy of the measurements was ensured by the verification of drug label and prescription. The population-based strategy adopted, the minimum loss of information on the medications used by the eligible participants, and uniform procedures for data collection between the cohorts ensured the reliability and internal validity of the study. Furthermore, to the best of our knowledge, this is

the first Brazilian population-based study that evaluated the trends in AD consumption among older adults.

In summary, the increased consumption of AD and the predominance of new generation drugs were consistent with findings observed in international studies of different populations and experimental designs. The positive association observed between AD consumption and income may indicate potential inequalities in accessing mental health services. Further studies employing different methodologies and designs (e.g., qualitative and longitudinal epidemiological studies) are necessary to deepen knowledge concerning AD use among older people. Furthermore, it can support interventions that will improve access to pharmaceutical care services with coverage and quality that are adequate for managing health problems of psychological origin in this population segment.

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